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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,487	01/30/2006	Alan Cuthbertson	PN0360	3640

36335 7590 04/24/2007

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IP DEPARTMENT
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EXAMINER	
AUDET, MAURY A	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,487	CUTHBERTSON ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/23/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-8,10 and 12-14* is/are pending in the application.

4a) Of the above claim(s) *9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7* is/are rejected.

7)☒ Claim(s) *2,4-6,8,10 and 12-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present application has been transferred from former Examiner Young to the present Examiner. The substance of the original search and examination was conducted by Examiner Young, and is being sent accordingly in the interests of compact prosecution (amended docket timeline). An updated search will follow.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-8, 10, and 12-14 as drawn to the species of moiety Z1 being an antineoplastic compound, in the reply filed on January 23, 2007 is acknowledged. Claims 9 and 11 are withdrawn from consideration as being drawn to non-elected subject matter.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "A compound of Formula (I)" in claim 1. There is insufficient antecedent basis for this limitation in the claim. The compound claimed in claim 7, as per the diagram included in claim 7, is drawn to a peptidomimetic structure with two sulfide bridge structures: an inner one with a disulfide linkage and an outer one with a monosulfide or

thioether linkage. *The compound of claim 1*, from which claim 7 depends, claims the compound of Formula (I), which has an identical outer linkage, a monosulfide or thioether group, *but has an inner linkage or loop that has an alkylene or alkenylene moiety of 1-4 carbons in length that is intercalated in between the two sulfur atoms of the linkage loop.* This moiety of 1-4 carbons, R3, is claimed in definite terms that state that it "is" present, with no option or possibility that it is absent or may be deleted.

Observation

The present Examiner has gone through the original search and noted a large volume of work by one or more of the present Inventors directed to the similar subject matter compounds. The presently compounds of formula (I) as not per se found in any references (e.g. relevant particularly to Double Patenting); however, as Applicants is contains the best knowledge of the pending family of applications which may be related, Applicant is asked to disclose any information regarding the description/claiming of closely related compounds of formula (I) in any other related US or international applications.

Objections to the claims

Claims 2, 4-6, 8, 10, and 12-14 are objected to as being dependent upon a rejected base claim, but would be likely receive favorable consideration if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art of record was not found to reasonably teach or render obvious the compounds of Formula (I) of claim 1, Formula (Ia) of claim 3, or of Formula (V) of claim 12. The compound of claim 7 was

searched as per the structure diagram provided in the body of claim 7 and was not found to be reasonably taught or rendered obvious.

It is also noted that the International Authority in related PCT/GB2004/003150 held the same findings in the Search Report (only citing seven "A" references to the same subject matter, some of which were Applicant's earlier works) and Written Report, under the equivalent PCT article/rules (see above Search Report for Documents D1, D2, D3, and D7):

> Novelty and Inventive Step (Article 33(2)(3) PCT)
> The present application addresses bicyclic peptides having the amino acid sequence KCRGDCFC being substituted at the C-terminus with a PEGylated moiety, at the €-amino group with an antineoplastic agent, a chelating agent or a reporter group bound via a linker molecule of the PEG-type. The C-terminal cysteine sulfur is bound as thioether via a methylene carbonyl group to the N-terminus. The other cysteines are bridged via a S-(CH2)I.4-S link. Thesecompounds are also claimed as being used in radiopharmaceutical compositions, a method for in vivo diagnosis. A method of preparation is claimed too.
> D1, which considered representing the closest prior art, discloses compounds which differ only in the lack of the methylene groups between the sulfur atoms of the Cys-Cys bridge. The other prior art documents are more remote concerning the amino acid sequence as well as the nature of the bridges forming the cyclic peptides.
> The subject-matter of present claims 1-14 is therefore novel.
> Taking the disclosure of D1 into consideration, the problem underlying the present application is to be regarded as to provide further alternative bicyclic peptides which can act as targeting compounds in diagnosis and therapy of diseases related to VEGF, i.e. to neovascularisation, thereby being chemically robust against attacks to the bicyclic structure which stabilises the particular conformation (see also pages 5 to 6 of D1).
> The solution presented by the present application is the introduction of a methylene group linking the Cys sulfurs. This solution is not suggested by the closest prior art alone or in combination with any of the prior art documents D2 to D7. D3 discusses the influence of the ring size upon the activity of backbone cyclised radiolabelled somatostatin analogues but mentions explicitly that bridges involving side chains of the amino acids should be avoided in order to prevent negative effects on the ligand binding to the receptor. The teaching of this document leads the skilled person away from the proposed solution. The other documents do not even deal with the problem of the stability of conformationally constrained bicyclic peptides. The subject-matter of present claims 14 is thus considered involving an inventive step.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 04/14/2007

MAURY AUDET
PATENT EXAMINER